REMARKS

Claims 25-60 are currently pending. Claims 25, 29, 37, 42, 44, 46, 49 and 51 are amended herein. Support for the amended claims may be found throughout the specification and claims as filed. For example, see the specification at page 4, lines 1-9. No new matter has been added.

Amendments to the Claims

As the Examiner will note, the term "SEQ ID NO:1" has been amended in the proposed claims to read "SEQ ID NO:3." Prior to the present sequence listing changes, the most recently filed sequence listing (faxed to the Office on July 11, 2001) recites the parathyroid hormone N-terminal sequence: "VAL-SER-GLU-ILE-GLN-LEU-MET" as corresponding to SEQ ID NO:3, rather than SEQ ID NO:1. To address any ambiguity, the Applicants have intended to present claims including the amino acid sequence: "VAL-SER-GLU-ILE-GLN-LEU-MET" irrespective of the SEQ ID NO attached thereto (see e.g., specification at page 4, lines 1-9). This amendment seeks, in part, to conform the claims to the most recent sequence listing submitted in this matter.

Amendments to the Specification

The specification is amended herein to conform with the most recent sequence listing filed in this matter as well as with the corrections thereto in the attached pages. Further, in response to the Examiner's request, Figure 6 is corrected herein to indicate separate headings for the top and bottom Figures. Per the Examiner's request, Applicants submit substitute Figures 6A and 6B. Further, the Brief Description of the Drawings is amended herein to reflect the heading changes in Figure 6 and to indicate that Figure 6B includes a peptide sequence that is representative of SEQ ID NO:6. No new matter has been added.

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Sequence Listing Amendments an Support

The sequence listing has been corrected to be in compliance with the sequence rules requirements of 37 C.F.R. 1.821-1.825.

The undersigned hereby states that the paper copy and the computer readable form copy (CRF copy) of the substitute Sequence Listing, submitted in accordance with 37 C.F.R. §1.825(a) and (b), respectively, are the same and contain no new matter. Accordingly, entry of the substitute Sequence Listing into the above-captioned case is respectfully requested.

The present sequence listing is adequately supported in the specification as filed. For example, SEQ ID NO:1 finds support in the specification at page 1, lines 27-30. SEQ ID NO:2 finds support, for example, in the specification at page 1, lines 26-27; SEQ ID NO:3 finds support, for example, in the specification at page 4, lines 1-9; SEQ ID NO:4 finds support, for example, in the specification at page 7, line 27; SEQ ID NO:5 finds support, for example, in the specification at page 7, line 28; and SEQ ID NO:6 finds support, for example, in Figure 6 (now 6B).

CONCLUSION

Entry of the present amendments and allowance of the pending claims 25-60 is earnestly requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**".

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this

document to **Deposit Account No. 03-1952** referencing docket no. 532212000600. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: January 14, 2003 By: _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning at page 3, line 28 has been amended as follows:

The present invention relates to a method for detecting wPTH in a biological sample without detecting the non (1-84) large PTH fragment component of I-PTH, and in particular to a substantially pure monoclonal or polyclonal antibody or antibody fragment specific for the initial sequence for wPTH which comprises a domain for adenylate cyclase activation, VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO. [1] 3), wherein at least four amino acids in this sequence are part of the antibody reactive portion of the peptide. The method for measuring the amount of wPTH in a sample such as serum, plasma, or blood comprises four general steps which can vary depending upon whether one uses a first antibody or antibody fragment specific for the PTH peptide VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO. [1] 3), wherein at least four amino acids are part of the antibody reactive portion of the peptide either as a signal antibody or a capture antibody in conventional immunoassay formats. Used either as a signal antibody or as a capture antibody, enough antibody is added to bind all w-PTH present. Next, one allows the first antibody to bind to any wPTH present, thereby forming a complex. A specific binding label comprised of a second antibody and a conventional immunoassay label, such as chemiluminescent agents, colorimetric agents, energy transfer agents, enzymes, fluorescent agents, and radioisotopes, is used to label the complex, preferably at the N-terminal end of wPTH, and can be added either substantially simultaneously with the first antibody or subsequent thereto. Finally, one uses conventional techniques to measure the amount of labeled complex, and thereby calculate wPTH levels in the sample. If used as a signal antibody, then the first.

The paragraph, beginning at page 5, line 14 has been amended as follows:

FIGURES 6A and 6B [is a] are diagrammatic views showing binding of whole (1-84) PTH compared with interference from non (1-84) PTH fragments (e.g., (7-84) PTH (SEQ ID NO:6)) in conventional I-PTH assays.

The paragraph, beginning at page 7, line 26 has been amended as follows:

In order to make the signal antibody in the above assay, first one makes a synthetic PTH peptide corresponding either to hPTH (Ser - Val - Ser - Glu - Ile - Gln - Leu - Met), SEQ ID NO:4 , rat PTH (Ala -Val - Ser - Glu - Ile - Gln - Leu - Met), SEQ ID NO:[7] 5, or at least four amino acids in the common sequence, absent the first amino acid. The selected peptide can play two roles in making an assay, first as a specific antigenic source for creating a polyclonal antibody or monoclonal antibody source for signal antibody or capture antibody, and second as part of an affinity purification means for isolating the desired signal antibody or capture antibody.

The paragraph, beginning at page 9, line 28 has been amended as follows:

FIGURE 5 shows the results for 34 normal human serum samples from healthy subjects which were assayed both by the present wPTH IRMA and the above I-PTH assay. In every case, the level of wPTH detected by the IRMA is lower than that reported by the I-PTH assay, demonstrating the ability of the present IRMA to avoid detecting the interfering large, non (1-84) PTH fragments detected by the I-PTH assay. FIGURES 6A and 6B illustrate[s] how such interference can occur. An N-terminal PTH specific signal antibody which is not specific to the initial PTH peptide sequence, as in the present invention, can detect not only wPTH (as in [the

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upper part of] FIGURE 6A), but also can detect large, non (1-84) PTH fragments (as in [the lower part of] FIGURE 6B).

In the Claims:

Please amend the claims as follows:

25. (Amended) A substantially pure antibody or antibody fragment specific for an initial peptide sequence of whole parathyroid hormone [which comprises] wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:[1] 3), and wherein at least four amino acids in said initial peptide sequence are part of a reactive portion with said antibody.

29. (Amended) A method for measuring an amount of whole parathyroid hormone in a sample comprising:

a) adding to a sample a labeled antibody or antibody fragment specific for an initial peptide sequence of whole parathyroid hormone [which comprises] wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:[1] 3), and wherein at least four amino acids in said initial peptide sequence are part of a reactive portion to said labeled antibody;

b) allowing said labeled antibody to bind to whole parathyroid hormone present, thereby forming a complex; and

c) measuring the amount of said labeled complex to measure the amount of whole parathyroid hormone in said sample while not detecting an interfering non-(1-84) parathyroid hormone fragment.

37. (Amended) A method for measuring an amount of whole parathyroid hormone in a sample comprising:

a) adding to a sample a first antibody or antibody fragment specific for an initial peptide sequence of whole parathyroid hormone [which comprises] wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:[1] 3), and wherein at least four amino acids in said initial peptide sequence are part of a reactive portion to said first antibody;

b) allowing said first antibody to bind to whole parathyroid hormone present, thereby forming a complex;

c) labeling said complex by adding a second labeled antibody that specifically binds to a portion of whole parathyroid hormone other than said initial peptide sequence that binds to said first antibody to form a labeled complex; and

d) measuring the amount of said labeled complex to measure the amount of whole parathyroid hormone in said sample while not detecting an interfering non-(1-84) parathyroid hormone fragment.

42. (Amended) A method for measuring whole parathyroid hormone by a precipitating or turbidometric immunoassay comprising:

a) adding to a sample an antibody or antibody fragment specific for an initial peptide sequence of whole parathyroid hormone [which comprises] wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:[1] 3), and wherein at least four amino acids in said initial peptide sequence are part of an antibody reactive portion of said peptide, said antibody being attached to a colloidal particle or moiety which can be used to detect a signal change;

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b) allowing said antibody to bind to whole parathyroid hormone present, thereby forming a complex; and

c) measuring change in said signal due to the formation of said complex to measure whole parathyroid hormone in said sample while not detecting an interfering non-(1-84) parathyroid hormone fragment.

44. (Amended) A kit for assaying for whole parathyroid hormone comprising:

a) a substantially pure antibody or antibody fragment specific for an initial peptide sequence of whole parathyroid hormone [which comprises] wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:[1] 3), and wherein at least four amino acids in said initial peptide sequence are part of a reactive portion with said antibody; and

b) a labeling component that binds to whole parathyroid hormone, but not to said parathyroid hormone initial peptide sequence VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:[1] 3).

46. (Amended) A kit for assaying for whole parathyroid hormone comprising:

a) a substantially pure antibody or antibody fragment specific for an initial peptide sequence of whole parathyroid hormone [which comprises] wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:3 [No. 1]), and wherein at least four amino acids in said initial peptide sequence are part of a reactive portion with said antibody; and

b) a second antibody bound to a solid support and said second antibody is specific for a portion of whole parathyroid hormone that does not include the domain for adenylate cyclase activation.

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49. (Amended) A method for measuring an amount of a functional N-terminal parathyroid hormone fragment and whole parathyroid hormone in a sample comprising:

a) adding to a sample a first antibody or antibody fragment specific for an initial peptide sequence of whole parathyroid hormone [which comprises] wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:[1] 3), and wherein at least four amino acids in said initial peptide sequence are part of a reactive portion with said first antibody;

b) adding to said sample a second antibody or antibody fragment specific for a peptide comprising amino acid sequence 28 to 34 of human parathyroid hormone (SEQ ID NO:2), which comprises a domain for protein kinase C activation, wherein at least four amino acids in said peptide sequence are a reactive portion with said second antibody;

c) allowing said first antibody and second antibody, wherein at least one of which is labeled, to bind to N-terminal parathyroid hormone fragment or whole parathyroid hormone present in said sample, thereby forming a labeled complex; and

d) measuring the amount of said labeled complex to measure the amount of said functional N-terminal parathyroid hormone fragment and whole parathyroid hormone in said sample while not detecting an interfering non-(1-84) parathyroid hormone fragment.

51. (Amended) A method for differentiating between a person having substantially normal parathyroid hormone function and having hyperparathyroidism comprising:

a) obtaining a sample from a person to be tested;

b) contacting said sample with a substantially pure antibody or antibody fragment specific for an initial peptide sequence of whole parathyroid hormone [which comprises] wherein

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said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:[1] 3), and wherein at least four amino acids in said initial peptide sequence are part of a reactive portion with said antibody; and

c) assessing binding between said substantially pure antibody or antibody fragment and whole parathyroid hormone, if present in said sample, to measure whole parathyroid hormone level in said person, while not detecting an interfering non-(1-84) parathyroid hormone fragment, and to determine if said person has substantially normal parathyroid hormone function or has hyperparathyroidism.